Researchers block transmission of malaria in animal tests

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By disrupting the potassium channel of the malaria parasite, a team of researchers has been able to prevent new malaria parasites from forming in mosquitoes and has thereby broken the cycle of infection during recent animal tests.

By genetically altering the malaria parasite through gene knock-out technol-ogy, a research team consisting of scientists at the University of Copenha-gen and John Hopkins University, Baltimore, has prevented the parasite from going through the normal stages of its life cycle and developing a cyst (egg-like structure or occyst), which spawns new infectious parasites." As it is exclusively the parasites from these oocysts that can infect new individu-als, we were able to prevent the disease from being transmitted to the animals in our tests", explains Assistant Professor, Peter Ellekvist from the University of Copenhagen.

The findings have been published in the scientific journal *Proceedings of the National Academy of Sciences*, USA, (2008 105: 6398-6402).

The malaria parasite has an extremely complicated lifecycle, which starts with the fertilisation of the parasites male and female gametes and the formation of an oocyst, in the mosquito's stomach wall. The oocyst further de-velops into sporozoittes, which travel up the mosquito's salivary gland and from there are transmitted to people, when the mosquito secures its next blood meal. After residing for a short period in the liver cells, the parasites then infect the red blood cells, thereby wreaking havoc in the human body. The malaria parasites are able to

reproduce both through sexual reproduction when they inhabit a mosquito (and are transmitted to the host) and via asexual reproduction when they reside in the human body (replication in the host). For scientists to successfully counteract malaria, they must tackle both the transmission from person to person by the mosquitoes and the spread of the malaria parasites in the infected individual.

All animal and plant cells contain so-called ion channels. These are small pores which allow ions to move in and out through an otherwise impermeable cell membrane. The potassium channels are a sub-type of ion channel, found in all cells. Though the function of the potassium channels vary, they play a crucial role in a variety of biological processes, e.g. influencing the ability of the nerves to send electrical signals and the heart muscle to contract rhythmically.

Assistant Professor Peter Ellekvist explains that his interest in malaria led to a research collaboration with Professor Dan Klærke, who studies potassium channels at the University of Copenhagen. In collaboration with Professor Nirbhay Kumar and other colleagues from the Malaria Research Institute at John Hopkins University in Baltimore, the two researchers were able to manipulate the parasite's genes so as to ensure that the potassium channel no longer functioned. To their surprise, however, this intervention did not, in the first instance, appear to have any effect on the parasites.

"The gene knock-out parasites essentially killed the mice in the animal tests just as quickly as the "natural" parasites, that had not undergone genetic manipulation," explains Peter Ellekvist. "However, we found that the only parasites that were unable to reproduce sexually, were those with non-functioning potassium channels."

The experiments had effectively disrupted the insect's ability to pass on the disease.

The next step for the research team is to examine whether parasites with non-functioning potassium channels react differently to anti-malaria drugs. A success here would allow the researchers to break the second phase of the infection cycle and prevent the asexual reproduction of the malaria parasites that have already gained access to the human body.

Blocking the potassium channels of parasites in the body could, for example, render them more susceptible to anti-malaria drugs. Further testing is also required to see whether the manipulation of the potassium channels may also affect the other stages of the parasites lifecycle, such as their development within the liver cells.

Source: University of Copenhagen